

### REMARKS

Claims 1-17 are pending in the present application. Claims 18-30 have been withdrawn by the Examiner as being drawn to a non-elected invention.

Claim 1 has been amended herein to recite that the presence of a *Chlamydia pneumoniae* infection in the central nervous system of a mammal, wherein the mammal does not exhibit symptoms of multiple sclerosis or meningoencephalitis, is assessed and, if the mammal has such infection, treatment is administered therefor.

Support for this amendment is present throughout the specification as filed, commencing on page 30, line 9, including, but not limited to, page 50, line 22, to page 51, line 8. Therefore, no new matter has been added by way of this amendment.

#### Rejection of Claims 1-17 Under 35 U.S.C. § 103(a)

Claims 1-17 stand rejected under 35 U.S.C. §103(a) as being obvious in view of U.S. Patent No. 5,424,187 ("Shor"). Applicants respectfully submit that claims 1-17 are not in any way obvious for the reasons set forth below.

Claims 1-7 recite a method of treating a *Chlamydia pneumoniae* infection in the central nervous system (CNS) in a mammal wherein the mammal does not exhibit symptoms of multiple sclerosis (MS) or meningoencephalitis. Claims 8-17 relate to methods of treating Alzheimer's disease (AD) in a mammal having a *Chlamydia pneumoniae* infection comprising administering an anti-microbial agent to treat the *C. pneumoniae* infection thereby treating the AD in the mammal.

Applicants respectfully submit that the disclosure of Shor does not render claims 1-17 *prima facie* obvious under 35 U.S.C. § 103(a) because the three-prong test that must be met under the statute to establish a case of *prima facie* obviousness has not been satisfied by the disclosure of Shor. More specifically, the MPEP states, in relevant part:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. MPEP § 2142.

None of these requirements has been satisfied in the instant matter.

As noted above, Shor describes the use of a macrolide antibiotic to treat an arterial *Chlamydial* granuloma. That is, Shor discovered a new disease, arterial *Chlamydial* granuloma, wherein *Chlamydial* infection of cells of the arterial wall is associated with arterial narrowing and/or arterial wall weakening and aneurysms. Shor does not teach or suggest treatment of a *Chlamydial* infection in the CNS; indeed, Shor does not even mention *C. pneumoniae* infection of the CNS at all. Instead, Shor relates to diagnosis and treatment of arterial *Chlamydial* granuloma which is a circulatory disease by detecting a marker specific for *Chlamydia* and a second marker specific for granuloma.

Nonetheless, the Examiner contends that a person of ordinary skill in the art would have been motivated to treat any *Chlamydial* infection using the methods of Shor (*i.e.*, using a macrolide or a macrolide in combination with an anti-inflammatory agent). Even assuming, *arguendo*, that this assumption is correct, the fact that the skilled artisan would have treated a *C. pneumoniae* infection using a macrolide, alone or combined with an anti-inflammatory agent, does not render claims 1-7 *prima facie* obvious. This is because Shor does not teach or suggest all of the claims limitations. Amended claim 1, from which claims 2-7 depend, now recites that the method comprises assessing the presence of a *C. pneumoniae* infection in the CNS. Literal support for this amendment is found throughout the specification as filed commencing at page 30, line 9. Moreover, the skilled artisan would have understood, based upon the disclosure provided in the specification as filed, that the invention encompasses assessing the presence of a *C. pneumoniae* infection in the CNS prior to administering anti-microbial treatment to treat such an infection. To do otherwise would be to blindly administer treatment to patients that may not suffer from such an infection and the skilled artisan would have understood, based upon the disclosure provided in the specification as filed, that assessing the presence of a *C. pneumoniae* infection in the CNS is encompassed in the invention.

Shor does not teach or suggest treatment of a *C. pneumoniae* infection in the CNS. Further, Shor does not teach or suggest assessing the presence of a *Chlamydial* infection in the CNS of a mammal. Therefore, Shor cannot render the present invention *prima facie* obvious under 35 U.S.C. §103(a) since it does not teach or suggest all of the claims limitations.

In addition, since Shor does not even mention, much less provide an enabling disclosure of, methods of treating a *C. pneumoniae* infection in the CNS, the skilled artisan

would not have been motivated to apply the teachings of Shor to arrive at the present invention recited in claims 1-7. Thus, one skilled in the art, based upon the disclosure of Shor, would not have been motivated to treat a CNS *C. pneumoniae* infection or even to look for one. Instead, as pointed out previously elsewhere herein, Shor is concerned with diagnosis and treatment of an arterial *Chlamydial* granuloma. Therefore, there would have been no suggestion or motivation, either in Shor or in the knowledge generally available to one of ordinary skill in the art, to modify Shor to treat a *C. pneumoniae* infection in the CNS.

Further, there would not have been any reasonable expectation of success in applying the teachings of Shor to treat a *C. pneumoniae* infection in the CNS. This is because, as pointed out previously elsewhere herein, there is nothing in Shor to suggest that there could be a *C. pneumoniae* infection in the CNS. Thus, Shor cannot render claim 1, as amended, and claims 2-7 depending therefrom, *prima facie* obvious under 35 U.S.C. §103(a).

Therefore, for the afore-mentioned reasons, Applicants respectfully submit that Shor cannot render claims 1-7, as amended, *prima facie* obvious under 35 U.S.C. §103(a), and the rejection of claims 1-7 on this basis should be reconsidered and withdrawn.

Applicants respectfully point out that the rejection of claims 8-17 under 35 U.S.C. §103(a) based upon Shor is even more improper than the rejection of claims 1-7 on the basis of this reference. More specifically, claims 8-17 recite methods of, *inter alia*, treating Alzheimer's disease in a patient also having a *C. pneumoniae* infection in the CNS where the patient does not have symptoms of meningoencephalitis or MS. Until the present invention, it was unknown and unexpected that there was a causal link between *C. pneumoniae* infection in the CNS and Alzheimer's disease. More importantly, no such connection is taught or suggested in the teachings of Shor.

The Examiner has apparently dismissed this deficiency in the teachings of Shor by arguing that treatment of *C. pneumoniae* infection using the method of Shor would inherently treat infection of *C. pneumoniae* in the CNS (notwithstanding the well-known difficulties associated with delivery of compounds across the blood-brain barrier pointed out by Applicants in response to the previous Office Action in this application). Even assuming, for argument's sake, that any technical hurdles associated with delivery of therapeutic agents across the blood-brain barrier could be overcome without undue experimentation based upon the limited teachings

of Shor, Applicants respectfully submit that the Examiner has confused inherency and obviousness and that Shor cannot render claims 8-17 obvious under the current law.

It is settled law that “the inherency of an advantage and its obviousness are entirely different questions. That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.” *In re Shetty*, 195 USPQ 753, 757 (CCPA 1977)(citing *In re Adams*, 148 USPQ 742 (CCPA 1966)). That is, “inherency is quite immaterial if the record establishes that one of ordinary skill in the art would not appreciate or recognize that inherent result.” *Adams*, 148 USPQ at 756 (quoting *In re Naylor*, 152 USPQ 106, 108 (CCPA 1966)). Thus, where a prior art method of combating microbial infection was also effective to curb appetite, such method of curbing appetite was patentable since it would not have been appreciated or recognized that a method of treating a microbial infection produced the appetite reducing effect. *See Shetty*, 195 USPQ at 756-57.

Similarly, in *In re Marshall*, 198 USPQ 344 (CCPA 1978), the Court of Customs and Patent Appeals reversed the PTO Board of Appeals and held that claims to a weight control process comprising administering an anesthetic, oxethazaine, to inhibit release of the pancreatic secretory hormones thereby preventing adsorption of food, were neither anticipated nor rendered obvious by claims reciting methods of using oxethazaine to treat esophagitis, gastritis, peptic ulcer and irritable colon syndrome. In finding that the claims at issue were not anticipated, the *Marshall* Court reasoned that “[n]othing in the PDR [Physician’s Desk Reference] remotely suggests taking oxethazaine to lose weight. If anyone ever lost weight by following the PDR teachings it was an unrecognized accident. An accidental or unwitting duplication of an invention cannot constitute an anticipation.” *In re Marshall*, 198 USPQ at 346 (emphasis added). Further, with regard to the obviousness rejection, the court stated:

The problem with this [Section 103 obviousness] rejection is that nowhere in any reference is there any suggestion to control weight by turning off the production and release of pancreatic enzymes. Although it has long been known that pancreatic enzymes are involved in digestion, from this record it appears that applicant is the first to suggest controlling weight by decreasing the quantity of pancreatic enzymes in the small intestine. To say this would have been obvious is to resort to impermissible hindsight.

*Id.* at 346-47. Thus, where the benefit of an old process would not have been anticipated or obvious, the new use of a known process is patentable. *See Chisum, Chisum on Patents* §1.03 at

1-58; accord *In re Woodruff*, 16 USPQ2d 1934 (Fed. Cir. 1998); *Mehl/Biophile International Corp. v. Milgraum*, 47 USPQ2d 1248 (D.N.J. 1998). See also *Howes v. Great Lakes Press Corp.*, 679 F.2d 1023, 1029, 216 USPQ 1049 (2d Cir. 1982) (holding that “a process or method which involves only a new use of an old material is patentable” and finding the invention patentable where applicant had created a new use of a known process).

More recently, in *Integra LifeSciences I Ltd. v. Merck KGaA*, 50 USPQ2d 1846 (D.S.Ca. 1999), the U.S. District Court for the Southern District of California discussed inherency in the context of anticipation under 35 U.S.C. §102. The Court held that a patent claiming inhibition of cell proliferation using a particular peptide was anticipated by a publication disclosing inhibition of cell attachment to a fibronectin matrix using the same peptide. The *Integra* Court, discussing *Ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App. & Int. 1993)<sup>1</sup>, reiterated the reasoning of *Shetty, supra*, and *Marshall, supra*, in that obviousness based on inherency depends not on what was actually observed, but on what would have been observed upon further inquiry into the results of the method at issue. *Integra*, 50 USPQ2d at 1851. Thus, the *Integra* Court held that since a simple additional observation would have revealed that the peptide that inhibited attachment also inhibited cell proliferation, and where substantially similar, if not identical steps, were recited in both methods, the reference disclosing inhibition of attachment anticipated methods of inhibiting cell proliferation using the same peptide. *Id.* at 1850-51.

Applicants respectfully submit that, under the present case law regarding inherency, Shor does not render claims 8-17, or claims 1-7, *prima facie* obvious under 35 U.S.C. § 103(a). Shor discloses treatment of arterial *Chlamydial* granuloma by administering certain compounds. Shor makes it clear, at column 2, lines 1-2, that tetracyclines and macrolides were well-known art-recognized compounds effective for treatment of *Chlamydia pneumoniae*

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<sup>1</sup> In *Ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App. & Int. 1993), the court held that a method of protecting a plant from pathogenic nematodes comprising inoculating the plant with *Pseudomonas cepacia* type Wisconsin 526, was anticipated by a method of inhibiting fungal growth comprising the exact same process steps. However, the court held that the anti-fungal method did not render the nematocidal method obvious. In any event, the present facts differ from *Novitski* in that the present invention does not involve use of the same steps to kill a different pathogen. That is, the instant invention does not relate to using the method of Shor to kill a different pathogen. Instead, the present invention relates to treatment of an entirely different illness, *i.e.*, Alzheimer's disease, by administering a macrolide, alone or with an anti-inflammatory agent, which treats an underlying *Chlamydial* infection in the CNS, where nothing in the prior art suggests or teaches that a *Chlamydial* infection in the CNS is associated with Alzheimer's disease.

respiratory infections. Based on these teachings, one of ordinary skill in the art would not have applied the teachings of Shor to treat Alzheimer's disease because, until the present invention, it was not known that *C. pneumoniae* infection in the CNS was involved in AD pathology such that treating the *Chlamydial* infection would treat Alzheimer's. These surprising teachings were heretofore unknown and no amount of additional observation of the effects of macrolides and anti-inflammatory agents in arterial *Chlamydial* granuloma patients would have revealed that such treatment would be effective against Alzheimer's disease. This is not a simple extension of the observations such as was the case in both *Novitski* and *Integra*, discussed previously herein. Rather, like the surprising results in *Shetty* and *Marshall*, the correlation between *Chlamydial* infection in the CNS and Alzheimer's disease could not be predicted based upon the teachings of Shor.

Although it may have been, *arguendo*, inherent that treatment of a systemic *Chlamydia* infection might treat Alzheimer's disease, such result was not known and was not obvious to one of ordinary skill based upon the teachings of Shor. That is, to paraphrase the *Marshall* Court, if anyone ever improved from Alzheimer's disease by following the teachings of Shor, it was an unrecognized accident. *Marshall*, 198 USPQ at 346. Thus, to say that this would have been obvious to one of ordinary skill armed with the teachings of Shor is impermissible hindsight.

Because Shor does not teach or suggest all of the claims limitations, and because there would have been no motivation to apply the teachings of Shor, nor any reasonable expectation of success in doing so, to treat Alzheimer's disease, Shor cannot render claims 8-17 *prima facie* obvious under 35 U.S.C. §103(a). Further, even assuming, *arguendo*, that the method of Shor would treat a *C. pneumoniae* infection in the CNS, it would not have been obvious to one of ordinary skill that the treatment would thereby treat Alzheimer's disease. Therefore, for the above-stated reasons, Shor cannot render claims 8-17 obvious under 35 U.S.C. §103(a) and this rejection should be reconsidered and withdrawn.

Remarks regarding Advisory Action mailed September 19, 2000 (Paper No. 12)

In the Advisory Action mailed on September 19, 2000 (Paper No. 12), refusing to enter the Amendment filed on September 8, 2000, the Examiner contends that it would have been obvious to one of ordinary skill in the art to treat an Alzheimer's disease patient having a

*Chlamydia pneumoniae* infection with anti-Chlamydia drugs. Applicants respectfully submit that

Even assuming, *arguendo*, that this statement is correct, this is not dispositive of the issue under consideration herein. That is, whether it was obvious to treat a *Chlamydia* infection in the lungs of a patient using known anti-chlamydia drugs, is not relevant where Applicants are claiming a method of treating a *C. pneumoniae* infection in the CNS where it was not known, prior to Applicants' invention, that *C. pneumoniae* infection could be localized in the CNS especially where the patient does not exhibit symptoms of multiple sclerosis or meningoencephalitis. This is because, prior to Applicants' discovery that *C. pneumoniae* infection in the CNS is involved in Alzheimer's pathology, it would not have been obvious to the skilled artisan to look for, much less to treat, a *C. pneumoniae* infection in the CNS where the patient does not present MS or meningoencephalitis symptoms.

Therefore, art-recognized methods for treatment of *C. pneumoniae* infection cannot render the present invention *prima facie* obvious where it was not known that *C. pneumoniae* infection could be present in the CNS and, with regard to claims 8-17, where it was not known that *C. pneumoniae* infection in the CNS plays a role in Alzheimer's disease. Assuming, for argument's sake, that it would have been obvious to treat a *C. pneumoniae* infection using anti-chlamydia drugs, it would not have been obvious that such an infection would be present in the CNS and it would have been even more surprising that treating a *C. pneumoniae* infection in the CNS would treat Alzheimer's disease.

For these reasons, and for the reasons set forth previously elsewhere herein responding to the Office Action mailed June 8, 2000 (Paper No. 10), Applicants' respectfully submit that claims 1-17 are not *prima facie* obvious and that the rejection of these claims under 35 U.S.C. §103(a), should be reconsidered and withdrawn.

Summary

For the foregoing reasons, the Applicants respectfully contend that each of claims 1-17 is in condition for allowance. Reconsideration and withdrawal of the Examiner's rejections and allowance of claims 1-17 is respectfully requested at the earliest possible time.

Respectfully submitted,

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